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DOI: <https://doi.org/10.1515/raon-2016-0005>

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ZORA URL: <https://doi.org/10.5167/uzh-135081>

Journal Article

Accepted Version

Originally published at:

Cotic, Jasna; Jamsek, Jure; Kuhar, Milan; Hren, Natasa Ihan; Kinsky, Andrej; Özcan, Mutlu; Jevnikar, Peter (2016). Implant-prosthetic rehabilitation after radiation treatment in head and neck cancer patients: a case-series report of outcome. *Radiology and Oncology*:1-7.

DOI: <https://doi.org/10.1515/raon-2016-0005>

Implant-prosthetic rehabilitation after radiation treatment in head and neck cancer patients:
a case-series report of outcome

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ABSTRACT

Introduction

Slovenia has a high burden of head and neck cancer. Patients are mostly treated with surgery followed by radiation therapy. Advanced surgical and prosthodontic techniques have expanded the rehabilitation options. The aim of the study was to review the outcome of implant-prosthetic treatment after radiation therapy.

Materials and methods:

20 irradiated head and neck cancer patients who received a removable implant-supported denture at the University Medical Centre Ljubljana were included in the study. Kaplan-Meier survival analysis, Cox proportional hazard models and logistic regression were used to assess the implant survival and success rate.

Results:

20 patients had 100 implants inserted. The estimated survival rate was 96% after 1 year and 87% after 5 years. Failures were mostly observed before loading (91.2%). Implants inserted in the transplanted bone were significantly more likely to fail. Out of 89 implants supporting the dentures, 79 implants (88.7%) were successful, meaning that they were functionally loaded and exhibited no pain, radiolucency or progressive bone loss. Prosthetic treatment was significantly less successful in older patients. The attachment system and the number of the denture did not have a statistically significant influence on the success rate.

Conclusions:

Implant-supported dentures proved to be a reliable treatment modality after head and neck cancer surgery and radiation therapy. Possible early failures should be communicated with the patients.

KEY WORDS

head and neck cancer, radiation therapy, dental implants, implant-supported dentures

Izid implantatno-protetične rehabilitacije po obsevanju zaradi raka glave in vratu

POVZETEK

Uvod:

V Sloveniji je visoka pojavnost raka glave in vratu. Zdravljenje najpogosteje vključuje kombinacijo kirurške obravnave in obsevanja. Možnosti kasnejše protetične rehabilitacije so izboljšane ob uporabi sodobnih kirurških tehnik in zobnih vsadkov. Namen prispevka je prikazati izid implantatno-protetične oskrbe obsevanih pacientov na Univerzitetnem kliničnem centru Ljubljana.

Metode in materiali:

V študiji smo preverili izid zdravljenja 20 pacientov po kirurški oskrbi in obsevanju zaradi raka glave in vratu, ki smo jih oskrbeli z implantatno podprtimi protezami. Preživetje in uspešnost zobnih vsadkov smo statistično ovrednotili z metodo Kaplan-Meier, Coxovimi modeli sorazmernih tveganj in logistično regresijo.

Rezultati:

20 pacientov je skupno prejelo 100 zobnih vsadkov. Ocenjena stopnja preživetja vsadkov je bila 96% po 1 letu in 87% po 5 letih. Do odpovedi vsadkov je večinoma prišlo pred obremenitvijo (91.2%). Vsadki v presajeni kosti so imeli statistično značilno slabše preživetje. Izmed 89 obremenjenih vsadkov jih je bilo 79 (88.7%) uspešnih, kar je pomenilo funkcionalno uporabo protez in odsotnost bolečin ali napredujoče izgube kostnine. Opazili smo statistično značilno slabšanje uspeha z napredujočo starostjo, medtem ko izbor protetičnega sidra in število vsadkov pod protezo in na uspeh rehabilitacije nista imela statistično značilnega vpliva.

Zaključki:

Implantatno podprte proteze so zanesljiv način protetične oskrbe po obsevanju zaradi raka glave in vratu. Paciente je potrebno seznaniti z možnostjo zgodnje odpovedi vsadkov.

INTRODUCTION

Slovenia is among the countries with the highest incidence of oral and oropharyngeal cancer (de Camargo Cancela, 2010 and 2012). In a population of 2 million people, approximately 450 cases are diagnosed per year (Cancer in Slovenia 2011, 2015). Most tumors are regionally advanced and the patients are treated with radical resection and reconstruction followed by radiation treatment (Cancer in Slovenia 2011, 2015). Afterwards, patients experience profound changes in the oral anatomy, function and facial appearance. Radiation treatment causes irreversible damage to both hard and soft tissues by creating a hypoxic, hypocellular and hypovascular environment which impedes wound healing and creates a risk for osteoradionecrosis (Marx, 1983). A protocol involving hyperbaric oxygen treatment (HBO) was proposed as a method to enhance wound healing by increasing the tissue oxygenation (Larsen, 1997).

Following the radical procedures to eradicate cancer, the greatest problems perceived by irradiated patients are swallowing, mouth opening, xerostomia and compromised aesthetics (Fierz, 2013). Prosthodontic treatment is advocated to regain lost oral functions, enhance the physical appearance and enable the patient to take part in normal daily activities with greater confidence. However, comprehensive prosthetic treatment after head and neck cancer is challenging, time-consuming and costly. Therefore, only 40% of such patients are treated following the postsurgical prosthetic protocol. Among them, 70% receive dentures supported by the residual teeth and bone and 30% receive implant-supported dentures (Brauner, 2010). Edentulous patients with head and neck cancer after radiation therapy are an especially vulnerable subgroup. Radiation treatment sequelae persist throughout the patient's lifetime and in the past, radiation therapy used to be an absolute contraindication

to placing of dental implants (Carini, 2012). Treatment options have therefore been limited to conventional complete dentures or no prosthetic rehabilitation at all.

Advanced surgical and prosthodontic techniques, such as 3D planning and guided implant surgery, have expanded the treatment options (Schiegnitz, 2014). In addition to conventional ball- and bar-retained dentures, new attachments have been introduced to clinical practice. Locator attachment is commonly used in removable implant prosthodontics. It is a self-aligning system with relatively simple maintenance requirements (Andreiotelli, 2010). Locator is, however, a non-rigid type of attachment and does not completely relieve the stress from the underlying mucosa. To address this issue, technically more advanced system of prefabricated double crowns on implants has been introduced (May, 2002). The SynCone system (Dentsply, Germany) is indicated in unfavourable resection areas, where completely rigid constructions are necessary due to the anatomical constraints. Both Locator and Syncone systems are commonly used at the University Medical Centre Ljubljana, Slovenia. These attachment systems have expanded the treatment possibilities for the rehabilitation of head and neck cancer patients, which is always a collaborative work between oral surgeons and prosthodontists.

The aim of the study was to review the outcome of the implant-prosthetic rehabilitation of irradiated patients performed at the University Medical Centre Ljubljana.

MATERIALS AND METHODS

A retrospective chart review was performed for the patients who were treated jointly by the Department of oral and maxillofacial surgery and the Department of prosthodontics at the University Medical Centre Ljubljana in the time period from 2008 to 2014. Only patients who underwent resection of malignant tumours with a subsequent radiation treatment and received removable implant-supported dentures were included in the study. The recorded data included patient gender and date of birth, smoking status at the time of prosthetic rehabilitation, cancer type, surgical management, date and dose of radiation treatment, administration of hyperbaric oxygen treatment (HBO), timing to implant surgery and to functional loading, treated jaw, type of implant bed, number of implants supporting the dentures, implant system and the denture attachment system used. At University Medical Centre Ljubljana, HBO is provided according to the protocol suggested by Marx and Larsen (Marx 1983, Larsen 1997). Patients are scheduled for 20 sessions before and 10 sessions after the implant insertion, respectively. Each 90-minute session consists of exposure to 100% oxygen on 2.5 ATA (1.5 bar) with three breaks during which patients breathe normal air.

The implants were assessed for survival and success using the guidelines proposed by van Steenberghe et al (1997). The survival criteria included osseointegration and presence in the mouth. To be considered successful, the implant had to be functionally loaded, immobile, without persistent pain or inflammation of the periimplant tissue and without progressive bone loss evident from radiographs and probing depth at yearly recall.

The survival time was measured from the date of the implant insertion to the date of the implant failure or the last control of the implant.

The present series consisted of 20 patients (11 men and 9 women) with a median age of 57.6 years (range 46.7 to 77.2 years) at the time of the implant insertion. 17 patients (85%) had a history of squamous cell carcinoma. Mucoepidermoid, adenoid cystic and origo ignota metastatic cancer were diagnosed in 1 patient each. The most common sites of primary cancer were the tongue and the floor of the mouth (6 patients each), followed by pharynx and maxilla (2 patients each). Mandible, tonsilla, larynx and origo ignota metastases in lymph nodes were encountered in one patient each. A segmental resection of the mandible was performed in 8 patients. In one patient, the tumor resection in the maxilla resulted in an oronasal communication. After surgery, all patients were subjected to the radiation therapy, with reported doses ranging from 54 to 66 Gy.

Reconstruction with bone and soft tissue grafts was accomplished in 3 patients. In two cases the fibular graft was used to reconstruct the mandible. In one patient the maxilla was reconstructed with the iliac crest bone graft.

The Kaplan-Meier method was utilized to estimate the implant survival rate. The association between the survival and the potential prognostic factors was analyzed by fitting univariate Cox proportional hazards models. The association between the potential prognostic factors and implant success was analyzed with univariate logistic regression models. The Holm-Bonferroni method was used to account for multiple comparisons and the level of significance was set to $\alpha=0.05$. Statistical analyses were conducted with the statistical software package R [R].

RESULTS

As presented in Table 1, 100 implants of 3 different implant systems were included in the study: 18 Astra Tech implants (Dentsply, Mannheim, Germany), 22 Straumann implants (Institut Straumann AG, Basel, Switzerland) and 60 Ankylos implants (Dentsply, Mannheim, Germany). 28 implants were inserted in the maxilla and 72 in the mandible. 92 implants were inserted in native bone and 8 in transplanted bone. The median time between the end of the radiation therapy and the implant surgery was 3.8 years (range 1.1 to 38.1 years).

Prophylactic antibiotic therapy was prescribed to all patients and HBO was administered to 16 patients. Osteoradionecrosis was not observed in this study. All implants were inserted in edentulous jaws, with 5 patients receiving implants in both jaws, 14 only in the mandible and 1 only in the maxilla. 12 patients were non-smokers and 8 patients were smokers at the time of the prosthetic rehabilitation. A two-stage implant insertion protocol was used in all cases. The median healing period between the implant insertion and functional loading was 15.1 months (range 4.3 to 54.3 months). As shown in Table 2, three different attachment systems for implant-supported dentures were used: 39 Locator attachments (Zest Anchors, Escondido, USA) (Figure 1), 40 prefabricated conical crowns (SynCone, Dentsply Friadent, Mannheim, Germany) (Figure 2), and 10 custom designed bar-clip systems.

Median follow up after implant insertion was 61.9 months (range 1.4 to 90.2 months).

The Kaplan-Meier estimated 1- and 5-year cumulative implant survival rates were 96% (95% confidence interval: 92.2%-99.9%) and 87.0% (95% confidence interval: 80.4-94.2%). The survival curve is shown on Figure 3. During the examination period, three patients died. Time of these 14 implants' service in the mouth was, as with other implants, registered from the date of the implant insertion to the date of the last follow-up examination.

The median time of failure was 19.1 months (range 1.4 to 48.5 months) after implantation.

The crude survival rate in our sample was 88%, as 12 implants in 5 patients failed. Data for all the implants and for the subgroups of survived and failed implants are described in Table 1. Primary implant failure during the healing period before functional loading was recorded in 11 implants (91.2%). The causes of implant removal in our sample were incomplete osseointegration (4), persistent pain (4), and periimplantitis with recurrent soft tissue hyperplasia (3). The only implant that was lost after functional loading (secondary implant failure) was included in a bar-supported denture and had to be removed because of periimplantitis.

Results of the analysis with the Cox regression models is presented in Table 2. The survived and failed implants were comparable considering the patient's gender, age and smoking status, the time elapsed between the radiation therapy and the implant surgery, the jaw of the implant insertion and the administration of HBO. The results for the bone type indicated that the implants inserted in the transplanted bone were statistically significantly more likely to fail than those inserted in the native bone. The influence of the implant system on the survival could not be analyzed because of the insufficient number of failure events among the three groups.

As presented in Table 3, 89 implants were observed after functional loading. 79 of those implants (88.7%) were successful, meaning that they were functionally loaded and exhibited no pain, radiolucency or progressive bone loss evident from radiographs and probing depth at yearly recall. Regardless of the appropriate osseointegration, prosthetic rehabilitation of 10 implants (11.2%) in four patients (20%) did not have a favourable outcome. Two patients with 4 implants experienced difficulties in adapting to dentures and did not wear them on regular basis. In addition, two further implants were considered unsuccessful because of persistent soft tissue discomfort reported by the patients. As shown in Table 3, higher

patient age was a statistically significant predictor for the lack of success. Gender, smoking status, healing time after implant insertion, the number of implants supporting the denture, the prosthetic system, jaw, bone type and administered HBO did not have a statistically significant effect on the success rate of loaded implants in this sample of irradiated patients.

DISCUSSION

It has been shown in this study that the implant-supported denture is a reliable treatment modality for the head and neck cancer patients that undergo radiation therapy. When special surgical and prosthodontic protocols are conducted appropriately, dental implants greatly enhance the stability of the dentures and improve the facial contours. According to the current guidelines, very few absolute contraindications exist for using dental implants in medically compromised patients (Diz, 2013). Radiation therapy in the head and neck region is no longer a contraindication, as there is a growing number of reports that a high osseointegration rate and a predictable treatment outcome can be expected (Ihde, 2009, Tanaka, 2013). When considering the prosthodontic rehabilitation options, the socio-economic status of the patients should be evaluated carefully. As head and neck cancer is connected with smoking and alcohol overconsumption, similar problems can persist after the initial cancer treatment, jeopardizing the implant-prosthetic rehabilitation outcome. In this case series of irradiated patients, the implant failures were rare and mostly confined to the healing period. The predominantly early implant loss is in accordance with the findings of Linsen et al (2012). Extended healing time should therefore be allowed after implantation and immediate loading protocols are not advised (Diz, 2013).

The Kaplan-Meier estimated 1- and 5-year cumulative implant survival rates were 96% and 87%. This is in accordance with Buddula et al (2012) reporting implant survival rates of 98.9% and 89.9% after 1 and 5 years and Yerit et al (2006) reporting a 95% and 91% survival after 2 and 5 years, respectively. Due to the small number of failed implants, detailed statistical analysis of prognostic factors for implant failure is often not possible or lacks power. It is therefore difficult to draw meaningful conclusions from the results of single studies alone. In this study, some limited insight could be obtained regarding the survival of implants. There

was a statistically significant higher failure rate in the transplanted bone. The reduced survival of implants in the transplanted bone may be explained by differences in bone quality, bone volume, and revascularization compared to the native bone (Schiegnitz, 2014). Our findings are in agreement with Yerit et al (2006), where lower survival was also reported for the transplanted bone. In contrast, Buddula et al (2012) reported no difference between implant survival in the native and transplanted bone. They also reported no difference in survival between genders and considering the time span between radiation treatment and implant insertion, which is in accordance with this study. Their finding of the statistically significant higher hazard ratio for implants in the upper jaw could not be confirmed in this study. While the risk for implant failure is known to be slightly greater in smoking patients (DeLuca 2006), the smoking status was not a detectable predictor for the implant survival in this study. This was also true for HBO, which is commonly used at the University Medical Centre Ljubljana for the head and neck cancer patients requiring surgery. Generally, there is no agreement on the HBO efficacy and value (Spiegelberg, 2010).

Implant osseointegration and survival data provide valuable information about the success of the implant therapy. Nevertheless, the final judgement of the implant-prosthetic therapy should be made according to the denture performance in the oral cavity. Successful implants enable the patients to use the dentures and do not cause any persistent discomfort. To achieve a favorable clinical outcome, it is crucial to design a viable prosthetic plan early in the rehabilitation process. Head and neck cancer patients present severely altered and unfavourable tissue conditions, making it challenging to model rehabilitation using the optimal top-down approach. The fragile mucosa, xerostomia, limited mouth opening and jaw deviations are additional factors to consider. The possible locations,

angulations and implant dimensions might not be ideal and should be discussed thoroughly between the oral surgeon and the prosthodontist.

The optimal number of implants should be carefully decided. There is a tendency to insert as few implants as possible in oncological patients, to facilitate bone healing. On the other hand a greater number is often required to design rigid, implant-borne prosthetic constructions (Diz, 2013). More implants also allow more flexibility in prosthetic treatment planning. Moreover, if some implants are lost, implant dentures can be successfully repaired and worn by the patients. It is currently thought that the number of implants is not critical for the success of the prosthetic treatment (Roccuzzo, 2012), but long-term clinical studies are lacking. In the present study the number of implants supporting the dentures was not a detectable factor in the success rate of the prosthodontic rehabilitation. Similarly, neither was the treated jaw or the healing time, which exceeded 4 months in all implants.

The loaded implants also exhibited similar success rates regardless of the denture attachment system used. While the bar-supporting implants experienced less success, the differences in comparison to the Locator attachments and SynCone systems were not significant.

Additional systemic and patient-related factors might play an important role in implant prosthetic rehabilitation. In this case series of irradiated patients, advanced age showed a negative prognostic value for the rehabilitation success, but not for implant survival. One of the possible limitations of this study was that the data on systemic diseases and alcohol consumption which might negatively affect implant performance were not included. After completion of the implant-prosthetic rehabilitation, it is of utmost importance to enrol the patient in an appropriate supportive program, with regular recalls, cancer screening and maintenance of the peri-implant conditions. The recall program should meet the individual

needs of the patients according to the overall risk profile. Some patients should be recalled every 3 months, while others may need to be checked once per year (Lang 2015).

This study has shown that favorable rehabilitation results can be obtained with implant-prosthetic treatment in irradiated patients. With proper collaboration between experienced surgeons and prosthodontists, this treatment modality can be regarded a viable option for oral rehabilitation after head and neck cancer.

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TABLES

Table 1

Summary of the implant survival according to the factors of interest.

Parameter	All implants (n=100)	Survived implants (n=88)	Failed implants (n=12)
Patient's median age at implant insertion in years (range)	58.3 (46.7-77.2)	61.5 (46.7-77.2)	57.9 (46.7-77.2)
Median time interval between radiation treatment and implant insertion in years (range)	3.8 (1.1-38.1)	3.2 (1.1-38.1)	5.2 (2.4-12.8)
Patient's gender <ul style="list-style-type: none"> Female, n (%) Male, n (%) 	40 (40%) 60 (60%)	32 (36%) 56 (64%)	8 (67%) 4 (33%)
Smoking <ul style="list-style-type: none"> No, n (%) Yes, n (%) 	66 (66%) 34 (34%)	57 (65%) 31 (35%)	9 (75%) 3 (25%)
Implant system <ul style="list-style-type: none"> Astra, n (%) Straumann, n (%) Ankylos, n (%) 	18 (18%) 22 (22%) 60 (60%)	18 (20%) 17 (20%) 53 (60%)	0 (0%) 5 (42%) 7 (58%)
Jaw <ul style="list-style-type: none"> Lower, n (%) Upper, n (%) 	72 (72%) 28 (28%)	63 (72%) 25 (28%)	9 (75%) 3 (25%)
Bone <ul style="list-style-type: none"> Native, n (%) Transplanted, n (%) 	92 (92%) 8 (8%)	85 (97%) 3 (3%)	7 (58%) 5 (42%)
HBO administred <ul style="list-style-type: none"> No, n (%) Yes, n (%) 	19 (19%) 81 (81%)	14 (16%) 74 (84%)	5 (42%) 7 (58%)

Table 2

Predictors of the implant failure.

Parameter	Hazard ratio (95% confidence interval)	<i>p</i>
Patient's age at implant insertion in years	1.05 (0.99-1.12)	1.0000
Time interval between the radiation treatment and the implant insertion in years	0.99 (0.92-1.07)	1.0000
Female gender	2.74 (0.82-9.10)	1.0000
Smoker	0.72 (0.19-2.66)	1.0000
Lower jaw	0.84 (0.23-3.09)	1.0000
Transplanted bone	12.37 (3.87-39.56)	0.0003
HBO administered	0.31 (0.10-0.98)	0.4753

Table 3

Summary of the loaded implants' success according to the factors of interest.

Parameter	All loaded implants (n=89)	Successful loaded implants (n=79)	Unsuccessful loaded implants (n=10)
Median patient's age at prosthetic rehabilitation in years (range)	59.1 (49.3-79.2)	58.9 (49.3-67.9)	71.7 (59.1-79.2)
Median healing time after the implant insertion in months (range)	15.1 (4.3-54.4)	15.2 (4.3-54.4)	13.0 (4.3-24.6)
Patient's gender <ul style="list-style-type: none"> Female, n (%) Male, n (%) 	33 (37%) 56 (63%)	25 (32%) 54 (68%)	8 (80%) 2 (20%)
Smoking <ul style="list-style-type: none"> No, n (%) Yes, n (%) 	57 (64%) 32 (36%)	49 (62%) 30 (38%)	8 (80%) 2 (20%)
Median number of the implants supporting the denture (range)	4 (2-5)	4 (2-5)	4
Implant denture system <ul style="list-style-type: none"> Bar, n (%) Locator, n (%) SynCone, n (%) 	10 (11%) 39 (44%) 40 (45%)	6 (8%) 37 (47%) 36 (45%)	4 (40%) 2 (20%) 4 (40%)
Jaw <ul style="list-style-type: none"> Upper, n (%) Lower, n (%) 	25 (28%) 64 (72%)	21 (27%) 58 (73%)	4 (40%) 6 (60%)
Bone <ul style="list-style-type: none"> Native, n (%) Transplanted, n (%) 	86 (97%) 3 (3%)	76 (96%) 3 (4%)	10 (100%) 0 (0%)
HBO administred <ul style="list-style-type: none"> Yes No 	75 (84%) 14 (16%)	65 (82%) 14 (18%)	10 (100%) 0 (0%)

Table 4

Predictors of the loaded implants' success.

Parameter	Odds ratio for the loaded implants' success (95% confidence interval)	<i>p</i>
Patient's age at prosthetic rehabilitation	0.66 (0.49-0.80)	0.0075
Healing time after the implant insertion	1.09 (0.53-2.73)	1.0000
Male gender	8.64 (1.99-60.09)	0.1456
Smoker	2.44 (0.57-16.95)	1.0000
Number of the implants supporting the denture	0.78 (0.24-1.94)	1.0000
Denture attachment system		
• Locator vs bar	12.33 (1.98-104.98)	0.1456
• SynCone vs bar	6.00 (1.15-32.68)	0.4416
• SynCone vs Locator	0.48 (0.06-2.65)	1.0000
Upper jaw	0.54 (0.14-2.30)	1.0000

Figures

Figure 1

A clinical situation of a patient with the segmental resection of the left mandible body due to cancer, as visible on the radiograph (a). The patient received an implant-supported lower denture (b), where the retention was based on the Locator concept (c).

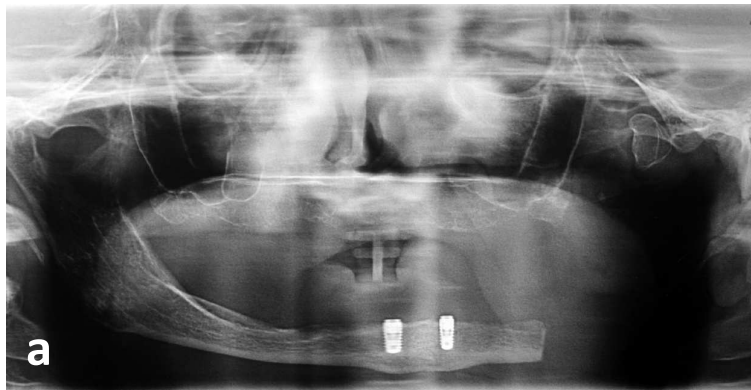


Figure 2

A clinical situation of a patient rehabilitated after oropharyngeal carcinoma. Segmental resection of the left mandible body is visible on the radiograph (a). The patient received implant-supported lower and upper dentures with retention based on the SynCone double crown concept (b).

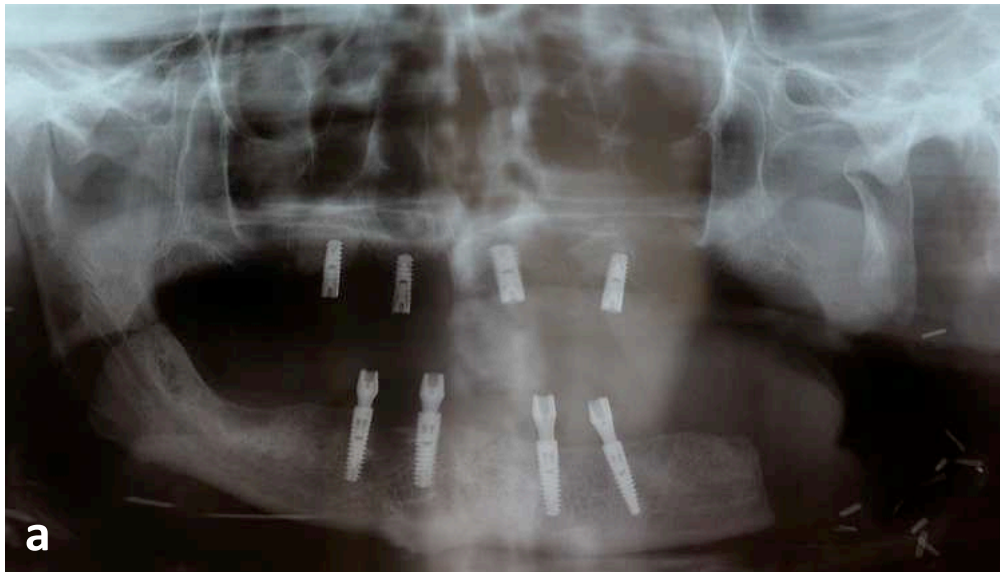


Figure 3

The Kaplan-Meier curve for the survival of the implants. 95% confidence intervals and censored data are included on the plot.

